

The opinion in support of the decision being entered today
is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte MAWAHEB M. EL-NAGGAR and AHMED S. MOUSA

Appeal 2007-2834
Application 09/943,048
Technology Center 1600

Decided: September 20, 2007

Before ERIC GRIMES, LORA M. GREEN, and RICHARD M.
LEBOVITZ, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a composition and method for treating inflammatory disorders. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

BACKGROUND

“One of the most adverse effects of nonsteroidal anti-inflammatory drugs (NSAIDs) is their ulcerogenic activity on the gastrointestinal tract”

(Specification 1). In contrast, “[f]lavonoids are shown to possess anti-inflammatory efficacy without the ulcerogenic side effects” (*id.*).

Treatment of inflammation with COX-2 selective inhibitors is also “associated with decreased incidence of adverse gastric events as a result of minimal inhibition of gastroprotective COX-1, but with equivalent anti-inflammatory benefit through inhibition of COX-2” (*id.* at 2). Despite the positive aspects of COX-2 inhibitor administration, “recent clinical reports suggested increased thrombotic events in patients taking COX[-]2 inhibitors suggesting the urgent need for the use of the COX[-]1 inhibitory efficacy of aspirin to improve such serious adverse outcome when using COX[-]2 inhibitors for long term” (*id.* at 2-3).

The Specification discloses “a method of preventing thrombotic complications due the long-term use of COX[-]2 inhibitors and to enhance its anti-inflammatory and anticancer efficacy by combining it with low dose enteric coated aspirin and flavanoids” (*id.* at 3).

DISCUSSION

1. CLAIMS

Claims 10-13, 15, and 18-24 are pending and on appeal. Claim 18 is representative and reads as follows:

18. A pharmaceutical composition, comprising a therapeutic composition for treating inflammatory disorders in a mammal, said therapeutic composition comprising: (i) a standard therapeutic dose of a COX[-]2 inhibitor selected from the group consisting of celecoxib and rofecoxib; (ii) low dose aspirin in an amount of 70-85 mg; and (iii) an antioxidant selected from the group consisting of a flavanoid, a flavonoid, an isoflavone, and combinations thereof.

2. PRIOR ART

The Examiner relies on the following references:

Hedden	WO 01/14705 A1	Jun. 28, 2001
Langhoff (as translated)	DE 198 55 426 A1	Jun. 8, 2000
Shapiro	US 6,444,221	Sep. 3, 2002
Burch	US 6,552,031 B1	Apr. 22, 2003
DRUG FACTS AND COMPARISON, 1995 EDITION, pp. 1248		
Hendler	US 6,541,613 B2	Apr. 1, 2003

3. OBVIOUSNESS -- CLAIMS 10-13, 18-21, 23, AND 24

Claims 10-13, 18-21, 23, and 24 stand rejected under 35 U.S.C. § 103(a) as obvious in view of Hedden, Langhoff, and Shapiro (Answer 6-7).

The Examiner cites Hedden as teaching “the use of [a] COX-2 inhibitor such as celecoxib and rofecoxib for the treatment of inflammatory disorders including arthritis” (*id.* at 6). The Examiner cites Langhoff as teaching “the use of low dose aspirin (in dosage range of 30mg-75mg) for the treatment of anti-inflammatory disorder including rheumatism and arthritis” (*id.*). The Examiner cites Shapiro as teaching “the use of flavonoids, flavanoids and isoflavones (i.e., daidzin, genistein, quercetin, silymarin, etc...) as antioxidants having functional equivalent property for the treatment of inflammatory disease conditions including arthritis or rhuematoidal arthritis” (*id.*).

Reasoning that Hedden, Langhoff, and Shapiro “make clear that COX-2 inhibitor[s] such as rofecoxib and celecoxib, low-dose aspirin and antioxidants (i.e., flavanoid, flavonoid and isoflavone) have been

individually used for the treatment of arthritis,” the Examiner concludes that it would have been obvious to combine those ingredients, “each of which is taught by [the] prior art to be useful for same purpose; [the] idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component” (*id.* at 7, citing *In re Kerkhoven*, 626 F.2d 846, 850 (CCPA 1980)).

Appellants argue that the cited combination of references fails to demonstrate the claims’ obviousness because Langhoff discloses that low dose aspirin has an anti-arthritis benefit only when co-administered with an ω -3-unsaturated fatty acid, vitamin E, and vitamin C (Br. 9-14),¹ and because “Shapiro teaches that the disclosed flavonoids, flavanoids and isoflavones as antioxidants are useful in treating [] inflammatory disease only in combination with carbonyl trapping agents” (*id.* at 20).

As stated in *In re Oetiker*, 977 F.2d 1443, 1445-1446 (Fed. Cir. 1992):

[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant.

. . . .

[T]he conclusion of obviousness *vel non* is based on the preponderance of evidence and argument in the record.

The test of obviousness is “whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention.” *In re Gorman*, 933 F.2d 982, 986 (Fed. Cir. 1991). Thus, “[i]t is impermissible

¹ Appeal Brief filed (August 29, 2006).

within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.” *In re Hedges*, 783 F.2d 1038, 1041 (Fed. Cir. 1986) (quoting *In re Wesslau*, 353 F.2d 238, 241 (CCPA 1965)). Moreover, “[a]s is clear from cases such as [*United States v. Adams*, 383 U.S. 39 (1966)], a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR Int’l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

In the instant case, Hedden discloses the use of celecoxib in compositions which are “especially useful as anti-inflammatory agents, such as in the treatment of arthritis” (Hedden 18). Hedden also lists rofecoxib as among COX-2 inhibitors useful in the compositions (*id.* at 16). Hedden’s compositions do not contain either the low-dose aspirin, or the flavanoid, flavonoid, or isoflavone, recited in claim 18’s composition.

However, Langhoff discloses that a composition containing 70-82 weight percent of an ω -3-unsaturated fatty acid, 7.5-13 weight percent of vitamin E, 10-15 weight percent of vitamin C, and 0.5-2 weight percent of acetylsalicylic acid (aspirin) is useful “in the treatment and prophylaxis of rheumatic and arthritic disorders” (Langhoff 3). Langhoff discloses that “the total quantity of acetylsalicylic acid . . . administered to the body is between 30 and 75 mg per day” (*id.*).

Langhoff discloses that “excellent” results were achieved in a patient suffering from “a rheumatic and/or arthritic disorder” by daily administering

5 grams of cod liver oil or linseed oil, 500 mg vitamin E, 500 mg vitamin C, and 40 mg of aspirin (*id.* at 8).² Thus, while Langhoff shows that the amount of aspirin recited in the composition of claim 18 would have been useful in a composition for treating an inflammatory disorder like arthritis, one of ordinary skill would have understood it to teach that the composition should also contain significant amounts of several other ingredients.

Shapiro discloses that chronic inflammatory disorders, including arthritis, can be treated by administering amine derivatives of benzoic acid, such as para-amino benzoic acid, “in combination with co-agents [including] clinically effective anti-oxidants” (see Shapiro, col. 7, l. 39 through col. 10, l. 26). Shapiro lists “daidzin . . . , genistein . . . , [and] quercetin” among antioxidants suitable for combination with the benzoic acid derivatives (*id.* at col. 20, ll. 47-54).

Shapiro states that the dosage of the benzoic acid derivative can “range from about 15 mg/kg/day to about 450 mg/kg/day” (*id.* at col. 10, ll. 54-55), and discloses an example in which an arthritis patient obtained therapeutic relief from daily administration of 2.2 grams per day of para-amino benzoic acid in combination with 800 I.U. of dl- α -tocopheryl acetate (an antioxidant) and 1 gram of L-methionine (*id.* at col. 25, l. 41 through col. 26, l. 46). Shapiro therefore teaches that the flavonoids or isoflavones recited in claim 18 should be combined with significant amounts of at least one other ingredient to achieve the desired anti-inflammatory effect.

² The amounts listed are based on Langhoff’s statement that composition “D” contained 50 percent of composition “A” and 50 percent of “B.”

One of ordinary skill reading the cited prior art as a whole would have reasoned from these teachings that obtaining a therapeutic effect from the ingredients recited in claim 18 would have required at least four ingredients in addition to those recited in the claim -- Langhoff's cod liver/linseed oil, vitamin C, and vitamin E, and Shapiro's benzoic acid derivative. As noted above, both the cod liver/linseed oil and benzoic acid derivatives are administered in multi-gram quantities to achieve a therapeutic effect.

We note that, because claim 18 uses the term "comprising" to describe the composition, the composition may contain the additional ingredients recited in the prior art compositions. *See Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501 (Fed. Cir. 1997) ("'Comprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.").

However, in the instant case, claim 18 requires all of the ingredients to be present in a single composition. As noted above, at least two of the ingredients taught in the art to be required for an anti-inflammatory effect, cod liver/linseed oil and para-amino benzoic acid, should be administered in multi-gram quantities. The Examiner has not adequately explained why one of ordinary skill would have included all of the different ingredients required in the prior art compositions, in the quantities disclosed in the prior art, in a single composition as recited in claim 18. We therefore do not agree with the Examiner that one of ordinary skill viewing the cited references would have considered the composition recited in claim 18 obvious.

Because the Examiner has not established a prima facie case of obviousness, we reverse the Examiner's rejection of claim 18 and its dependent claims 19-21 and 23.

Claim 10 essentially recites a method of treating inflammation in a mammal by administering the composition of claim 18. We therefore also reverse the Examiner's rejection of claim 10 and its dependent claims 11-13 and 24.

4. OBVIOUSNESS -- CLAIMS 15 AND 22

Claims 15 and 22 stand rejected under 35 U.S.C. § 102 as obvious over Hedden, Langhoff, and Shapiro in view of Burch, Drug Facts, and Hendler (Answer 7-8).

We will reverse this rejection as well. Claims 15 and 22 depend from claims 10 and 18, respectively. The compositions recited in claims 15 and 22 therefore contain the same ingredients recited in claims 10 and 18. As discussed above, we do not agree with the Examiner that Hedden, Langhoff, and Shapiro suggest a composition having the claimed ingredients. We do not see, and the Examiner does not point to, any disclosures in Burch, Drug Facts, or Hendler that remedy the shortcomings of the other references.

We therefore reverse the Examiner's rejection of claims 15 and 22.

SUMMARY

We reverse the Examiner's rejection under 35 U.S.C. § 103 of claims 10-13, 18-21, 23, and 24 as obvious in view of Hedden, Langhoff, and Shapiro. We also reverse the Examiner's obviousness rejection of claims 15 and 22.

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REVERSED

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